9. (Amended) The method of claim 4, wherein the transport agent component binds to and localizes to a molecule present on the luminal surface of caveolae of the luminal surface of the vascular endothelium.

Remarks

In order to expedite prosecution, Claim 1 has been canceled. Cancellation of Claim 1 eliminates the following Groups set forth in the Restriction Requirement: Groups 1, 2 and 3.

In addition, the claims have been amended to specify that the microdomain of interest is caveolae. These amendments remove caveolae associated with G domains; and G domains, from the claims. These amendments eliminate the following Groups set forth in the Restriction Requirement: Groups 2, 3, 5, 6, 8, 9, 11, 12, 17, 18, 19, 20, 21, 22, 23, 24, 305-584, and 585-864 as numbered by the Examiner.

The remaining Groups are: Groups 4, 7, 10, 13, 14, 15, 16, and 25-304 as numbered by the Examiner. Applicants' Attorney traverses this restriction of the invention.

The claimed invention is drawn to methods of delivering an agent of interest in a tissue-specific manner, in which the agent is delivered not solely to the tissue, but is in fact delivered into, and/or across the tissue, or even further. In the methods, an agent of interest is delivered into, and/or across a luminal surface of vascular endothelium, and/or from one side of an underlying cell to another side, in a tissue-specific manner, by targeting a component of caveolae. As can be seen in the Specification (see, for example, the Examples, particularly Example 9), Applicant has demonstrated the progressive movement of a desired agent into, and subsequently across a luminal surface of vascular endothelium. The claims reflect this progressive transport, and pertain to transport of a desired agent in relation to vascular endothelium. All of the claims describe methods which target a component of caveolae. A single art search relating to the commonality (such as an art search that pertained to use of components of caveolae for transport

of agents in relation to vascular endothelium) would provide the relevant references for the pending claims, without creating an undue search burden.

Furthermore, the division on the invention into so very many groups is unduly burdensome to the Applicant. According to the restriction requirement as originally presented by the Examiner, Applicant would be obligated to file close to 900 separate patent applications in order to protect the invention(s). Such a requirement has a chilling effect on the filing and prosecution of patent applications.

If the Examiner believes that a telephone conversation would expedite prosecution of the application, the Examiner is invited to contact Elizabeth W. Mata at (915) 845-3558 (Mountain time zone). If Elizabeth W. Mata cannot be reached, the Examiner is invited to contact Doreen M. Hogle at 978-341-0036.

Respectfully submitted,

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Dated: May 27, 2003

MARKED UP VERSION OF AMENDMENTS

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

2. (Amended) A method of delivering an agent of interest into and/or across a luminal surface of vascular endothelium in a tissue-specific manner, comprising the steps of:

a) selecting an agent of interest that binds to and localizes to a component of [a microdomain] caveolae of the luminal surface of the vascular endothelium upon contact with the luminal surface, wherein the component [of the microdomain] to which the agent binds and localizes is tissue specific[, and wherein the microdomain is selected from the group consisting of: caveolae, G domains, and caveolae associated with G domains]; and

b) contacting the luminal surface of vasculature with the agent of interest, thereby delivering the agent into and/or across the luminal surface of the vascular endothelium in a tissue-specific manner.

3. (Amended) A method of delivering an agent of interest across a luminal surface of vascular endothelium and from one side of an underlying cell to another side in a tissue-specific manner, comprising the steps of:

a) selecting an agent of interest that binds to and localizes to a component of [a microdomain] caveolae of the luminal surface of the vascular endothelium upon contact with the luminal surface, wherein the component [of the microdomain] to which the agent binds and localizes is tissue specific[, and wherein the microdomain is selected from the group consisting of: caveolae, G domains, and caveolae associated with G domains]; and

b) contacting the luminal surface of vasculature with the agent of interest, thereby delivering the agent across the luminal surface of the vascular endothelium and from one side of an underlying cell to another side in a tissue-specific manner.

4. (Amended) The method of Claim 3, wherein the agent of interest comprises an active agent component and a transport agent component, wherein the transport agent component binds to and localizes to a component of [the microdomain] caveolae of the luminal surface of the vascular endothelium.

9. (Amended) The method of claim 4, wherein the transport agent component binds to and localizes to a molecule present on the luminal surface of [a microdomain] caveolae of the luminal surface of the vascular endothelium.